

CLAIMS

1. A method for inhibiting plasma membrane UCP expression in a cell, comprising:

5 contacting a cell with a plasma membrane UCP inhibitor to inhibit plasma membrane UCP expression.

selection of species
← 2. The method of claim 1, wherein the plasma membrane UCP inhibitor is selected from the group consisting of a UCP binding peptide or molecule, an anti-UCP
10 antibody, a hydrophobic nucleotide analog, and a non-omega-3 fatty acid.

3. The method of claim 2, wherein the cell is a tumor cell.

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4. The method of claim 3, wherein the tumor cell is in a subject and wherein the
15 plasma membrane targeted UCP inhibitor is administered *in vivo*.

5. The method of claim 3, wherein the tumor cell is in a subject and wherein the plasma membrane targeted UCP inhibitor is administered *ex vivo*.

20 6. The method of claim 3, further comprising the step of administering to the subject a cytotoxic anti-tumor therapy.

7. The method of claim 6, wherein the cytotoxic anti-tumor therapy is radiation.

25 8. The method of claim 1, wherein the cell is a lymphocyte.

9. The method of claim 1, wherein the cell is a pancreatic β cell.

10. The method of claim 1, wherein the rapidly dividing cell is a bacteria.

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11. The method of claim 1, wherein the cell is a B cell.

~~12.~~ A composition, comprising:

a plasma membrane targeted UCP inhibitor.

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13. The composition of 12, wherein the UCP inhibitor is a nucleotide or nucleotide analog.

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14. The composition of claim 13, wherein the nucleotide analog is a purine analog.

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15. The composition of claim 14, wherein the purine analog is selected from the group consisting of guanosine diphosphate, 8-oxo-Adenosine, 8-oxo-Guanosine, 8-fluoro-Adenosine, 8-fluoro-Guanosine, 8-methoxy-Adenosine, 8-methoxy-Guanosine, 8-aza-Adenosine and 8-aza-Guanosine, azacitidine, Fludarabine phosphate, 6-MP, 6-TG, azathioprine, allopurinol, acyclovir, gancyclovir, deoxycoformycin, and arabinosyladenine (ara-A), guanosine diphosphate fucose, guanosine diphosphate-2-fluorofucose, guanosine diphosphate-.beta.L-2-aminofucose, guanosine diphosphate-D-arabinose and 2-aminoadenosine.

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16. The composition of claim 13, wherein the nucleotide analog is a pyrimidine analog.

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17. The composition of claim 16, wherein the pyrimidine analog is selected from the group consisting of uracil, thymine, cytosine, 5-fluorouracil, 5-chlorouracil, 5-bromouracil, dihydrouracil, 5-methylcytosine, 5-propynylthymine, 5-propynyluracil and 5-propynylcytosine, 5-fluorocytosine, Floxuridine, uridine, thymine,
5 3'-azido-3'-deoxythymidine, 2-fluorodeoxycytidine, 3-fluoro-3'-deoxythymidine;
3'-dideoxycytidin-2'-ene; and 3'-deoxy-3'-deoxythymidin-2'-ene, and cytosine arabinoside.

18. The composition of 12, further comprising a pharmaceutically acceptable
10 carrier.

19. The composition of claim 12, further comprising a colloidal dispersion system, wherein the plasma membrane UCP inhibitor is incorporated into the colloidal dispersion system.
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20. The composition of claim 19, wherein the colloidal dispersion system is a liposome.

21. The composition of claim 12 wherein the plasma membrane UCP inhibitor
20 includes a hydrophobic moiety.

22. The composition of claim 21, wherein the plasma membrane UCP inhibitor is a modified nucleotide analog conjugated to a hydrophobic moiety.

23. The composition of claim 22, wherein the plasma membrane UCP inhibitor
25 includes a membrane attachment domain

24. The composition of claim 23, wherein the plasma membrane UCP inhibitor is a membrane attachment domain conjugated to a nucleotide or nucleotide analog.

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25. The composition of claim 24, wherein the membrane attachment domain is a Type I membrane attachment domain.

26. The composition of claim 24, wherein the membrane attachment domain is a Type II membrane attachment domain.

5 27. The composition of claim 24, wherein the membrane attachment domain is a Type III membrane attachment domain.

28. The composition of claim 24, wherein the membrane attachment domain is selected from the group consisting of P-Cadherin

(FILPILGAVLALLLLLTLLALLLV); CD2 (IYLIIGICGGGSLLMVFVALLVIFYIT);

10 CD40 (ALVVIPIHFGILFAILLVLVFI); Contactin (ISGATAGVPTLLLGLVLPAP); IL-4 receptor (LLGVSVSCIVILAVCLLCYVSIT); Mannose receptor

(VAGVVIIIVILLILTGAGLAAYFFY); M-CSF receptor

(FLFTPVVVACMSIMALLLLLLLLLL); PDGFR .beta. chain

(VVVISAILALVVLTIISLIILIMLWQKKPR); PDGFR .alpha. chain

15 (ELTVAAAVLVLLVIVSISLIVLVVTW); P-Selectin

(LTYFGGAVASTIGLIMGGTLLALL); Rat Thy-1

(VKCGGISLLVQNTSWLLLLLSLSFLQATDFISL); TNFR-1

(TVLLPLVIFFGLCLLSLLFIGLM); and VCAM-1 (LLVLYFASSLIIPAIGMIIYFAR).

SUB
H1
20 29. A method for treating a cancer, comprising administering to a subject having a cancer the plasma membrane UCP inhibitor of any one of claims 12-28, in an effective amount to treat the cancer.

30. The method of claim 29, further comprising administering an anti-tumor therapy.

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SUB
H2
31. A method for preventing a cancer, comprising administering to a subject at risk of developing a cancer the plasma membrane UCP inhibitor of any one of claims 12-28 in an effective amount to prevent the cancer.

~~32.~~ A composition, comprising:

a UCP inhibitor associated with a lysosomal targeting molecule.

5 33. The composition of claim 32, wherein the UCP inhibitor is an anti-UCP antibody.

34. The composition of claim 33, wherein the anti-UCP antibody is conjugated to an anti-cell surface molecule antibody.

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~~35.~~ A composition, comprising:

a UCP associated with a plasma membrane targeting molecule.

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15 ~~36.~~ The composition of claim ~~32 or 35~~, further comprising a colloidal dispersion system, wherein the UCP inhibitor and the plasma membrane targeting molecule are incorporated into the colloidal dispersion system.

37. The composition of claim 36, wherein the colloidal dispersion system is a liposome.

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~~38.~~ A method for sensitizing a resistant tumor cell to a cytotoxic therapy, comprising:

expressing a functional UCP or UCP fragment in a plasma membrane of a resistant tumor cell to sensitize the resistant tumor cell to a cytotoxic therapy.

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39. The method of claim 38, wherein the method is performed in a subject having a cancer.

40. The method of claim 39, wherein the functional UCP or UCP fragment is administered to the subject in conjunction with a delivery vehicle.

41. The method of claim 40, wherein the delivery vehicle is a liposome.

42. The method of claim 39, wherein the functional UCP or UCP fragment is injected into a tumor of the subject.

43. The method of claim 39, wherein the functional UCP or UCP fragment is expressed in the plasma membrane of a cell of the subject by delivering to the subject a nucleic acid encoding the UCP or UCP fragment and a plasma membrane targeting sequence.

44. The method of claim 38, wherein the resistant tumor cell is a melanoma cell.

~~45.~~ A method for screening a tumor cell of a subject for susceptibility to treatment with a chemotherapeutic agent comprising:

isolating a tumor cell from a subject; and

detecting the presence of a UCP molecule in the plasma membrane of the tumor cell, wherein the presence of the UCP molecule in the plasma membrane indicates that the tumor cell is susceptible to treatment with a chemotherapeutic agent.

46. The method of claim 45, wherein the method comprises the step of contacting the tumor cell with a detection reagent that selectively binds to the plasma membrane UCP molecule to detect the presence of the plasma membrane UCP molecule.

5 47. The method of claim 45, wherein the plasma membrane UCP molecule is a plasma membrane UCP mRNA, the detection reagent is a nucleic acid that selectively hybridizes to the plasma membrane UCP mRNA and wherein the cell is contacted with the detection reagent under conditions that permit selective hybridization of the nucleic acid to the plasma membrane UCP mRNA.

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 48. The method of claim 45, wherein the plasma membrane UCP molecule is a plasma membrane UCP polypeptide, the detection reagent is a plasma membrane UCP binding peptide and wherein the plasma membrane UCP polypeptide is contacted with the detection reagent under conditions that permit selective binding of the plasma
15 membrane UCP binding peptide to the plasma membrane UCP polypeptide.

 49. The method of claim 48, wherein the plasma membrane UCP binding peptide is an anti-plasma membrane UCP polypeptide antibody.

20 50. The method of claim 48, wherein the presence of the plasma membrane UCP polypeptide is detected by contacting the tumor cell with a plasma membrane UCP binding peptide attached to a solid support.

~~51.~~ A method for screening a subject for the presence of rapidly dividing cells,
25 comprising:

 isolating a sample of cells from a subject; and,

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detecting the presence of a plasma membrane UCP molecule in the plasma membrane of the cell, wherein the presence of the plasma membrane UCP molecule is indicative of a rapidly dividing cell.

5 ~~52.~~ A kit for screening a tumor cell of a subject for susceptibility to treatment with a chemotherapeutic agent comprising:

a container housing a UCP molecule detection reagent; and

instructions for using the UCP molecule detection reagent for detecting the presence of a UCP molecule on the plasma membrane of the tumor cell, wherein the
10 presence of the plasma membrane UCP molecule indicates that the cell is susceptible to treatment with a chemotherapeutic agent.

53. The kit of claim 52, further comprising a container housing a chemotherapeutic agent.

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54. The kit of claim 52, further comprising a panel of chemotherapeutic agents, housed in separate compartments.

55. The kit of claim 52, wherein the UCP molecule detection reagent is attached
20 to a solid surface.

~~56.~~ A method for inducing cellular division in a growth arrested cell, comprising:
expressing a functional UCP or UCP fragment in a plasma membrane of a growth
arrested cell to induce cell division of the cell.

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57. The method of claim 56, wherein the growth arrested cell is a nerve cell.

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58. The method of claim 57, wherein the functional UCP or UCP fragment is administered to a subject in conjunction with a delivery vehicle.

5 59. The method of claim 58, wherein the delivery vehicle is a liposome.

Sub C3
~~60. A method for regulating lysosomal pH, comprising:
modifying lysosomal UCP activity in a cell to regulate lysosomal pH.~~

10 61. The method of claim 60, wherein the cell is a T cell.

62. The method of claim 61, wherein the cell is a neutrophil.

Sub A4
15 ~~63. The method of claim 61 or 62, wherein the lysosomal UCP activity is
modified by contacting the cell with a lysosomal UCP inhibitor.~~

Sub B2
20 ~~64. The method of claim 63, wherein the lysosomal UCP inhibitor is selected
from the group consisting of a dominant negative lysosomal UCP, and a lysosomal
targeted binding peptide or molecule.~~

65. The method of claim 60, wherein the lysosomal UCP activity is modified by contacting the cell with a lysosomal UCP activator.

Sub C3
~~66. A method for treating or preventing an infectious disease, comprising:~~

administering to a subject having or at risk of developing an infectious disease a lysosomal UCP inhibitor in an effective amount for treating or preventing the infectious disease.

C3
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5 ~~sub 2~~ 67. The method of claim 66, wherein the lysosomal UCP inhibitor is selected from the group consisting of a dominant negative lysosomal UCP, and a lysosomal targeted binding peptide or molecule.

10 68. The method of claim 66, further comprising administering an antigen to the subject.

69. The method of claim 68, wherein the antigen is selected from the group consisting of a viral, a bacterial, a parasitic, and a fungal antigen.

15 70. The method of claim 66, wherein the subject is infected with an intracellular pathogen.

71. The method of claim 70, wherein the intracellular pathogen is an intracellular bacteria.

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72. The method of claim 70, wherein the intracellular pathogen is an intracellular parasite.

~~73.~~ A method for treating autoimmune disease, comprising:

25 administering to a subject having autoimmune disease a UCP activator in an effective amount to prevent antigen presentation.

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74. The method of claim 73, wherein the UCP activator is a functional UCP or UCP fragment with a lysosomal membrane targeting molecule.

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